



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,945	01/09/2007	Katherine Weilbaecher	60005161-0217	4085

71902 7590 10/03/2008
WASHINGTON UNIVERSITY-SNR
C/O SONNENSCHN NATH & ROSENTHAL L.L.P
P.O. BOX 061080
WACKER DRIVE STATION , SEARS TOWER
CHICAGO, IL 60606

EXAMINER

RAO, SAVITHA M

ART UNIT	PAPER NUMBER
----------	--------------

1614

MAIL DATE	DELIVERY MODE
-----------	---------------

10/03/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,945	Applicant(s) WEILBAECHER ET AL.	
	Examiner SAVITHA RAO	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 and 23-42 is/are pending in the application.
- 4a) Of the above claim(s) 1-12, 15-17 and 25-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-14, 18-21 and 23-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/03/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-21 and 23-42 are pending and are subject of this office action.

Claims 1-12, 15-17 and 25-42 are withdrawn as being drawn to a non-elected invention

Claims 13-14 and 18-21 and 23-24 are under consideration in the instant office action

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 08/03/2007. The Examiner has considered the reference cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Election/Restrictions

Applicant's election with traverse of Group II (13-24) in the reply filed on 06/13/2008 is acknowledged. The traversal is on the ground(s) that a there is no serious burden in examination of these different claims and that the examiner has not shown that claimed group requires separate classification or separate status in the art or in a different field of search.

Examiner finds the applicant's argument unpersuasive and maintains the restriction. Examiner has appropriately pointed out that the restricted Groups do not share the same or corresponding technical feature and thereby lack unity of invention. Applicant is informed that as provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single

Art Unit: 1614

general inventive concept (“requirement of unity of invention”). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression “special technical features” shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Additionally, When Claims Are Directed to Multiple Categories of Inventions:

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

The instant application is drawn towards multiple independent method inventions and accordingly lack unity of invention. Thereby

Applicant's election with traverse of following species compound ML-464 recited in claims 24 and melanoma as a specific cancer cell type or specific tumor species is acknowledged. The traversal is on the ground(s) that there is no serious burden in examination of these different claims and that the examiner has not shown that claimed group requires separate classification or separate status in the art or in a different field of search.

Examiner does not find the applicant's argument wholly persuasive since the compounds encompassed in instant claims 20 and 21 (from the elected Group II) are numerous and encompasses different groups, for example, substituent options for Z, a spirocyclic nucleus in instant claim 20 includes tetracyclo, pentacyclo, hexacyclo and heptacyclo groups which comprises hetero-atoms, this results in compounds which are classified under US classes 549 (sulfur and oxygen containing heterocyclo), 548 (Five-membered heterocyclic ring with one or more nitrogen), 546 (six membered heterocyclic ring with one nitrogen), 544 (six-membered heterocyclic ring with at least 2 heteroatoms) and 540 (seven-membered or larger nitrogen containing heterocyclic rings).

With reference to compound election of specie, upon reconsideration, Examiner has expanded the search to include compound ML- 728 as set forth in instant claim 23 along with ML-464 of instant claim 24 as the only difference between the two compounds is the esterification of the carboxyl group.

The election of specie requirement for the tumor cell type is maintained.

Claims 1-12, 15-17 and 25-42 are withdrawn from further consideration pursuant

Art Unit: 1614

to 37 CFR 1.142(b), as being drawn to a nonelected inventions and specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/13/2008.

Thereby the restriction and election of specie requirement is still deemed proper and is therefore made FINAL

Claim Interpretation

With reference to instant claims 13-21 and 23-24, Examiner is interpreting the tumor cell being inhibited as the elected melanoma tumor cells and the organ system comprising the cells to be the tissue of origin. Since the tissue of origin for the applicant's elected tumor cell specie "melanoma" is the skin, **claims 15 and 17 which recite the skeletal system of the subject as the organ system are withdrawn from consideration.**

Claim Rejections - 35 USC § 112- 1st Paragraph: Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-21, 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of melanoma tumor cell growth in a subject, does not reasonably provide enablement for preventing the growth of melanoma cells. The specification does not enable any person skilled in the art to which

Art Unit: 1614

it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary, 2) the amount of direction or guidance provided, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the art, and 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to prevention and inhibition of melanoma tumor cell growth, and the relative skill of those in the art is high, generally that of a PHD or MD. This unpredictability has a number of facets, as discussed hereinafter.

A. Treatment by Cancer Type

While the state of the art is relatively high with regard to the treatment methods which inhibit specific tumor cell growth with specific agents, it has long been underdeveloped with regard to the prevention of tumor growth broadly. In particular,

Art Unit: 1614

there is no known agent which is effective to prevent all cancer. This is why the National Cancer Institute (NCI) has the extensive in vitro drug screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), in vitro assays are used by NCI (such as the melanoma cell line testing used in the instant case) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) Id. at 1567-68. These in vitro tests are considered reasonably correlative of success in vivo.

Thus, a considerable amount of in vitro empirical testing is required, with no a priori expectation of success being present, before a candidate anticancer agent can be considered useful to prevent any and all cancer.

2. The breadth of the claims

The claims are very broad and inclusive of prevention of melanoma cell growth generally. The term "prevention" can be construed broadly as either prevention of the growth of clinically evident tumors altogether or preventing the onset of a preclinically evident stage of neoplasia in individuals at risk. In other words, the instant claims are drawn to a composition and method of preventing all preclinical stages of any and all stages of tumor cell growth, which includes any undetectable stages of tumors.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, a priori, which part of the tumor cell growth will be prevented. It is known in the art that various factors are involved in tumor growth, including genetics and environmental factors, such as diet and exposure to carcinogens. Although working examples, i.e. experimental data demonstrating the tumor growth inhibiting activity of the claimed compounds are demonstrated, specification is silent as to examples demonstrating the prevention of tumor growth.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual prevention of all tumor cell growth in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which stage of tumor cell growth the claimed agents will be effective against without resorting to undue experimentation. Applicant's disclosure of examples demonstrating reduction of metastases in mice and inhibition of platelet aggregation by two compounds ML728 and ML464 is noted, but is not sufficient to claiming prevention of all tumor cell growth broadly.

Absent a reasonable a priori expectation of success for using a specific compound to treat any particular type of tumor, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation

Art Unit: 1614

would be required to practice the invention as it is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Amending the claims to recite "A method for inhibiting melanoma tumor cell growth..." instead of "preventing" would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is vague and indefinite in that the metes and bounds of the term "tumor cell is comprised by" are unclear. The (term/phrase) is unclear because "tumor cell is comprised by" indicates that the tumor cell consists of an organ system, as claimed in instant claim 14. Appropriate correction is recommended.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

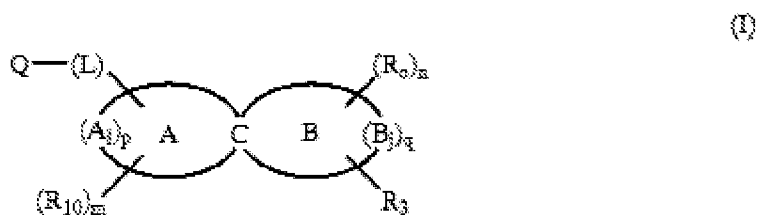
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-14, 18-21 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fisher et al (US 6291469, referenced in the instant IDS) in view of Pitts et al (US 6489333) further in view of Trikha et al (Cancer Research, vol. 57, pp 2522-2528 (1997)) .

Fisher teaches novel spiro compounds that block the GPIIb/IIIa fibrinogen receptor (same as $\alpha IIb\beta 3$ receptors as evidenced by Pitts and Trikha et al. secondary references used in this rejection), thereby inhibiting platelet aggregation and subsequent thrombus formation (col1, lines 40-43).

Art Unit: 1614

Fisher teaches certain spirocyclic compounds having a spiro nucleus formed from two fused rings A and B represented by the formula (I) below and all pharmaceutically acceptable salts, solvates and prodrug derivatives thereof (abstract and col.1, lines 49-61)

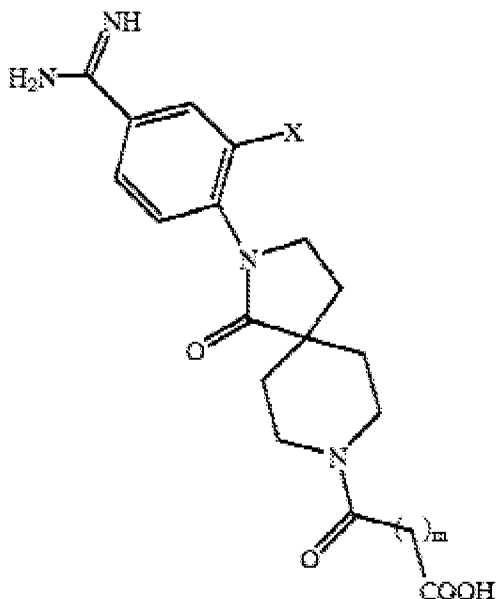


Fisher teaches compounds of formula (II) below



wherein Z is a spirocyclic nucleuse selected from (A) (B) (C) or (D) described in col.4, lines 35 to col. 5, lines 10.

Fisher teaches among one of the most preferred subset of compounds the following compound (col. 39, lines 49-65) where X is F or H, m is 0-4 (col.31, line 1)



Fisher teaches prodrugs of the compounds of his inventions which have metabolically cleavable groups and become by solvolysis or under physiological conditions the compounds of the inventions which are pharmaceutically active in vivo, for e.g., ester derivatives of the compounds are often active in vivo, but not in vitro (col. 43, lines 47-52). Fisher further teaches that simple aliphatic and aromatic esters derived from acidic groups, pendant on the compounds of his invention are preferred prodrugs (col. 43, lines 62-64). Finally Fisher teaches a method of preventing or treating thrombosis in mammals, especially humans, with therapeutically effective amount of the compound of his invention, indications of which includes arteriosclerosis, acute ischemic attacks and strokes, peripheral vascular disease, etc. (col.166, lines 40-56) and teaches other indications wherein the platelet aggregation inhibitors of his inventions have potential use for (col.167, lines 1-21).

Fisher is silent as to the use of the compounds with Spiro nucleus that inhibit $\alpha\text{IIb}\beta 3$ receptors in a method of preventing or inhibiting tumor cell growth in a subject.

However, Pitts et. al. teaches novel heterocycles which are useful as antagonists of the $\alpha\text{v}\beta 3$ and $\alpha\text{IIb}\beta 3$ integrin and related cell surface adhesive protein receptors and methods of using the compounds for the inhibition of cell adhesion, treatment of antigenic disorders, inflammation, bone degradation, cancer metastasis and other condition mediated by cell adhesion and/or cell migration and/or angiogenesis (abstract) Pitts teaches that Tumor dissemination, or metastasis, involves several distinct and complementary components, including the penetration and transversion of tumor cells through basement membranes and the establishment of self-sustaining tumor foci in diverse organ systems To this end, the development and proliferation of new blood vessels, or angiogenesis, is critical to tumor survival. Without neovascularization, tumor cells lack the nourishment to divide and will not be able to leave the primary tumor site (col.1, lines 36-44).Pits additionally teaches that inhibition of angiogenesis in animal models of cancer has been shown to result in tumor growth suppression and prevention of metastatic growth and many angiogenic inhibitors have been directed toward blocking initial cytokine-dependent induction of new vessel growth, e.g. antibodies to endothelial cell growth factors. Pitts also teaches that a general approach which would allow for inhibition of angiogenesis due to a variety of stimuli would be of benefit (col.1, lines 46-55). Pitts teaches that, since several endogenous agonists are involved in activating platelet function and aggregation, an inhibitor which acts against all agonist would represent a more efficacious antiplatelet agent than currently available anti-

Art Unit: 1614

platelet drugs which are agonist specific (col.3, lines 25-37) . Pitts additionally teaches a common pathway for all known agonists namely platelet glycoprotein IIb/IIIa complex (GpIIb/IIIa), a membrane protein mediating platelet aggregation which is a member of integrin family also referred to as fibrinogen receptor or the α IIb β 3 integrin (col.3, lines 46-51). Compounds taught by Pitts binds to integrin receptors thereby altering cell-matrix and cell-cell adhesion processes and are useful for the inhibition of cell adhesion and the treatment of cancer metastases among other indications. (col.4, lines 61-67).

Pitts does not teach α IIb β 3 antagonists being used for inhibition of tumor cell growth specifically melanoma cells growth.

However, Trikha teaches fibronectin-adherent melanoma cells possess an intracellularly localized pool of high-affinity α IIb β 3 receptors (abstract). Trikha teaches that integrins are cell surface receptors (α IIb β 3 and α v β 3) which mediate homotypic and heterotypic interactions among tumor cells and host cells in addition to tumor cell interactions with tumor cell-extracellular matrix (ECM) (page 2522, left col., 1st paragraph). Trikha teaches that the integrin α IIb β 3, originally termed as GPIIb-IIIa was initially identified in platelets and is directly involved in platelet aggregation and cell signaling and ligand binding to α IIb β 3 alters the state of intracellular kinases, GTPases and phospholipases (page 2522, right col. 2nd paragraph). Trikha also teaches that B16a murine melanoma cells expresses the α IIb β 3 integrin and that this receptor plays an important role in tumor cell-platelet, tumor cell-endothelial cell and tumor cell-ECM interactions (page 2522, right col. 3rd paragraph). Trikha demonstrates detection and

Art Unit: 1614

expression of $\alpha\text{IIb}\beta 3$ in three human melanoma WM 983B, WM 983A and WM 35 cell lines through several different *in-vitro* experimental procedures (page 2524 right col. 2nd paragraph) and demonstrated expression of $\alpha\text{IIb}\beta 3$ in melanoma tumors [skin melanoma specimens from two Hungarian woman aged 27 and 35 (page 2524, left col. 2nd paragraph)] through *in-vivo* studies (page 2526, left col. 2nd paragraph) and concludes that $\alpha\text{IIb}\beta 3$ can be detected in melanoma tumor *in-vivo* and cultured melanoma cells *in-vitro* and is capable of directly supporting melanoma cell adhesion as is involved in invasion (page 2527, right col. last paragraph).

In view of the foregoing references, the instantly claimed method for of inhibiting tumor cell growth with $\alpha\text{IIb}\beta 3$ inhibitors such as the instantly claimed spiro compounds would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Fisher discloses spiro compounds identical to the generic compounds claimed in instant claim 20 and 21 and compounds structurally similar to the instantly elected specie including the ester prodrug. Fisher additionally teaches the spiro compounds to be platelet-specific activated $\alpha\text{IIb}\beta 3$ receptor antagonists which inhibits platelet aggregation and thrombus formation. Pitts teaches use of compounds which are integrin receptors antagonists for inhibition of cell adhesion and the treatment of cancer metastases among other indications. Finally, Trkha demonstrates expression of $\alpha\text{IIb}\beta 3$ receptors both *in-vitro* in melanoma cells and *in-vivo* in melanoma tumor samples. Accordingly, an ordinarily skilled artisan would be motivated to use structurally similar compounds taught in the prior art to be $\alpha\text{IIb}\beta 3$ receptor antagonists that inhibits platelet aggregation, in a method to inhibit melanoma tumor growth. Pitts also teaches

Art Unit: 1614

solutions to the problem of using a agonist specific anti-platelet inhibitor in treatment procedures which is to a general approach which would allow for inhibition of angiogenesis due to a variety of stimuli such as using integrin receptor antagonists which alter cell-matrix and cell-cell adhesion processes and are useful for the inhibition of cell adhesion and the treatment of cancer metastases. This solutions to the prior art problem also provides the skilled artisan motivation to combine the references. An ordinarily skilled artisan will be imbued with at least a reasonable expectation of success that a method of treating melanoma tumors with spiro compounds that inhibit platelet aggregation will result in decrease in tumor growth and prevention of invasion.

Conclusion

Claims 13-14, 18-21 and 23-24 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614